REMARKS

Applicants appreciate the thorough examination of the present application as evidenced by the final Office Action dated May 17, 2005 (hereinafter, "Final Action").

Claims 1-19 and 21-27 are pending in the present application upon entry of the present Amendment. Claim 12 has been amended, and Claims 24-27 have been added. Applicants submit that the claim amendment and new claims do not present new matter, and Applicants respectfully request entry thereof.

The issues presented in the Final Action are addressed below.

I. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

A. Enablement Rejection

Claims 1-19 and 21-23 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. *See* Final Action, page 3. More specifically, the Final Action states that "[t]he specification, while being enabling for removing some prion molecules from a sample, does not reasonably provide enablement for the limitation 'such that the liquid is non-infective with respect to prion protein infectivity.'" Final Action, page 3.

In contrast to the assertion of the Final Action on page 3, determining the presence or absence of infectivity does not require knowledge of which model "actually is the correct one." Concerning the present invention, in view of the extent of prion protein removal, the resulting liquid is non-infective after treatment employing the methods recited in the claims of the present application. In particular, an article by Reichl et al. entitled "Studies on the removal of a bovine spongiform encephalopathy-derived agent by processes used in the manufacture of human immunoglobulin," *Vox Sanguinis* **83**:137-146 (2002), further demonstrates that the liquid is non-infective after treatment as recited in the present claims. The Reichl et al. article is cited on the Supplemental Information Disclosure Statement submitted concurrently herewith. Applicants respectfully submit that any burden of proof that the Applicants may have concerning the ability of the present methods to render an aqueous liquid non-infective with respect to prion protein infectivity as recited in Claim 1 has been met.

Accordingly, Applicants respectfully submit that Claims 1-19 and 21-23 are enabled, and Applicants request that the rejection under U.S.C. §112, first paragraph, as lacking enablement, be withdrawn.

B. Written Description

Claims 1-19 and 21-23 stand rejected under 35 U.S.C. §112, first paragraph, as lacking written description. *See* Final Action, page 4. The Final Action states that "[i]n this instance the specification does not provide a particular test that is to be employed in order to determine that the particular liquid is deemed non-infective." Final Action, page 4.

The present claims do not recite a method of determining prior protein infectivity. Instead, the present claims recite a method of removing abnormal infective prion proteins associated with transmissible spongiform encephalopies (TSEs). As noted above, use of the method can provide a liquid that is non-infective with respect to prion protein infectivity.

Accordingly, Applicants respectfully submit that Claims 1-19 and 21-23 comply with the written description requirement, and Applicants request that the rejection under U.S.C. §112, first paragraph, as lacking written description, be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 102

Claims 1-19, 21 and 22 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,407,212 to Morgenthaler et al. (hereinafter, "Morgenthaler et al."). *See* Final Action, page 5. More specifically, the Final Action states that "Morgenthaler et al. disclose a method of removing prion from a blood sample using filter binding agents which are selected from kieselguhr, perlite or diatomaceous earth and contacting the blood product with the filter binding agent before filtration of the liquid through a membrane filter." Final Action, page 6.

Claim 1 recites as follows:

> 1. A method of removal of abnormal infective prion proteins associated with transmissible spongiform encephalopies (TSEs) from an aqueous liquid containing a natural product, which comprises **passing the liquid through a depth filter formed of a matrix comprising solid particles of porous material and having a pore**

size providing a retention less than 6 μm, and so removing abnormal infective prion proteins which may be present in the liquid such that the liquid is non-infective with respect to prion protein infectivity.

Applicants respectfully submit that Morgenthaler et al. fails to teach or suggest at least the highlighted recitations of Claim 1. Instead, Morgenthaler et al. discusses a general process involving adsorption, filtration and/or centrifugation. Morgenthaler et al. does not teach or suggest a method employing a depth filter functioning and having the recited properties as recited in Claim 1. Independent Claims 17 and 18 present similar recitations. Anticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of **each and every** recitation of a claimed invention. *See Apple Computer Inc. v. Articulate Systems Inc.* 57 USPQ2d 1057, 1061 (Fed. Cir. 2000) (*relying on Electro Med. Sys. S.A. v. Cooper Life Scis.*, 32 USPQ2d 1017, 1019 (Fed Cir. 1994) (Emphasis added).

Accordingly, Applicants respectfully submit that Claims 1-19, 21 and 22 are not anticipated in view of Morgenthaler et al., and Applicants request respectfully that the rejection of these claims be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103

Claims 1-19 and 21-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 96/05846 to Nebe (hereinafter, "Nebe"), U.S. Patent No. 5,696,236 to Omar et al. (hereinafter, "Omar et al.") and EP 0798003A2 to Savage et al. (hereinafter, "Savage et al.") for reasons of record. *See* Final Action, page 7.

As previously noted in Applicants' Amendment dated July 26, 2004, the combination of the cited references fails to teach or suggest the present invention. More specifically, the examples of the present application show that there is **no detectable prion protein in the filtrate after filtration** according to the methods of the present invention. The examples further show that other types of filters, such as those employed in some of the cited references, were **not effective** in removing prion proteins. Results are summarized in Table 1 on page 14 of the specification.

In stark contrast, Nebe shows that the pre-filter removed only half of the infectious agent enabling the liquid to transmit prion protein disease to the patient.

The filters employed by Nebe were **not effective** in removing prion proteins, where nearly five logs of infectivity/ml passed through the filters as shown on page 13 of Nebe.

The current Final Action continues to cite Omar et al. and Savage et al. to cure the deficiencies of Nebe. Yet, neither Omar et al. nor Savage et al. cure the deficiencies of Nebe. Both Omar et al. and Savage et al. are concerned with the removal of **viruses** and not **prion proteins**. Omar et al. discusses a method for the removal of **viruses** from protein solutions. *See* Col. 1, lines1-2. Savage et al. discusses removing **viruses** from solutions. *See* page 5, line 5. As noted in the present application on page 2, paragraph 1 through page 3, paragraph 1, prions are known to be abnormal proteins having infectious capacity. While viruses also have infectious capacity, the virus infection is governed by a completely different mechanism than prion infection. See, for example, Flint et al., *Principles of Virology: Molecular Biology, Pathogenesis, and Control*, ASM Press, **15-17** (2000), and Riesner, "Biochemistry and structure of PRP^{C} and PrP^{Sc}," *British Medical Bulletin* **66:21-33** (2003) (copy previously submitted). Thus, Applicants respectfully submit that one of ordinary skill in the art would not rely upon Savage et al. and/or Omar et al., which are clearly directed to treatment of viruses and not prion proteins, to address the problem of improving the **ineffective prion removal rate** disclosed in Nebe. Thus, one of ordinary skill in the art would not be motivated to combine the cited references **without knowledge of the present invention** elucidating a method for removal of removal of abnormal infective prion proteins associated with transmissible spongiform encephalopies (TSEs).

Accordingly, Applicants respectfully submit that Claims 1-19 and 21-23 are not obvious in view of the cited references, and Applicants request that the rejection of these claims be withdrawn.

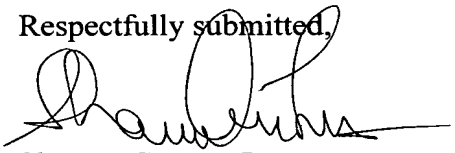
Conclusion

Applicants respectfully submit that, for at least the reasons discussed above, the rejection of the claims have been overcome. Accordingly, Applicants respectfully request allowance of all the pending claims and passing this application to issue. The Examiner is respectfully requested to contact the undersigned directly should there be

any remaining rejections after review of this Amendment. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

It is not believed that any fee(s), including fees for additional claims, are required, beyond those that may otherwise be provided for in documents accompanying this paper including the Petition and Fee for Extension of Time and the Request for Continued Examination. In the event, however, that additional fees are necessary to allow consideration of this paper, such an extension is also hereby petitioned for under 37 C.F.R. §1.136(a). Applicants authorize that any additional fees believed to be due in connection with this paper may be charged to Deposit Account No. 50-0220.

Respectfully submitted,



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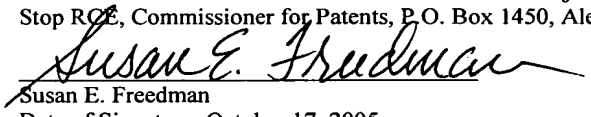

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Date of Signature: October 17, 2005